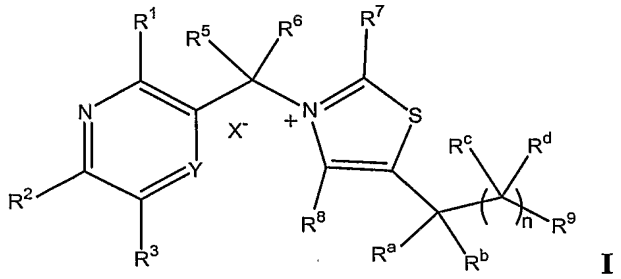
What is claimed is:

1. A compound of formula **I**:



I

or a pharmaceutically acceptable derivative thereof, wherein:

Y is N or $C(R^4)$;

R^1 is H, alkyl, $-N(R)_2$, $-(CH_2)_{1-6}N(R^\circ)_2$, $-(CH_2)_{1-6}OR^\circ$, -NRC(O)R, $-C(O)N(R)_2$, -CN, $-NRSO_2R$, -COOR, -OR, -SR, -C(O)R, halo, -OC(O)R, -NRC(O)OR, $-OC(O)N(R)_2$, -NRC(O)NR, -NRC(S)NR, $-NRSO_2NR$, $-C(O)NRN(R)_2$, heteroaryl, or heterocyclyl;

each R^2, R^3 and R^4 is independently H, alkyl, fluoroalkyl, -C(O)R, -COOR, $-C(O)N(R)_2$, -CN, -NRC(O)R, -OR, -SR, $-N(R)_2$, $-(CH_2)_{1-6}OR^\circ$, $-(CH_2)_{1-6}N(R^\circ)_2$, or halo;

each R^5 and R^6 is independently H, alkyl, or fluoroalkyl;

R^7 is H, alkyl, fluoroalkyl, aralkyl, carbocyclylalkyl, heterocyclyl, carbocyclyl, heterocyclylalkyl, aryl, heteroaryl, heteroaralkyl, -C(O)R, $-(CH_2)_{1-6}OR$, $-(CH_2)_{1-6}N(R)_2$, $-C(O)CH_2C(O)R$, -NRC(O)R, $-N(R)_2$, $-C(O)N(R)_2$, or -C(H)(OR)R;

R^8 is H, alkyl, fluoroalkyl, carbocyclyl, carbocyclylalkyl, heteroaryl, heterocyclyl, $-CO_2R$, or $-CON(R)_2$;

R^9 is $-OR^{10}$ or $-NR^{11}R^{12}$;

R^{10} is R°, -C(O)R, $-C(O)N(R)_2$, -C(O)OR, $-(CH_2)_{1-6}$-C(O)R, $-PO_3M_x$, -P(O)(alkyl)OM', $-(PO_3)_2M_y$, carbocyclyl, aryl, heterocyclyl, heteroaryl, carbocyclylalkyl, aralkyl, heterocyclylalkyl, heteroaralkyl, or a tumor-targeting moiety;

x is 1 or 2;

y is 1, 2 or 3;

each M is independently H, Li, Na, K, Mg, Ca, Mn, Co, Ni, Zn, or alkyl;

M' is H, Li, Na, K, or alkyl;

R^{11} is H or alkyl;

R^{12} is H, alkyl, -C(O)R, -C(O)N(R_2), -C(O)OR, -SO_2R, -SO_2N(R_2), carbocyclyl, aryl, heterocyclyl, heteroaryl, carbocyclylalkyl, aralkyl, heterocyclylalkyl, heteroaralkyl or a tumor targeting moiety;

each R^a and R^b is independently H, OR°, alkyl, or fluoroalkyl;

each R^c and R^d is independently H, alkyl, or fluoroalkyl;

n is 0-4;

X^- is a monovalent or divalent anion, or a counterion to the thiazolium nitrogen located anywhere in the molecule;

R° is H or alkyl; and

R is R°, carbocyclyl, aryl, heterocyclyl, heteroaryl, carbocyclylalkyl, aralkyl, heterocyclylalkyl, or heteroaralkyl;

provided that the following compounds are excluded:

Y is C(R^4);

R^5, R^6, R^a, R^b, R^c and R^d are H;

R^8 is methyl;

R^9 is -OR^{10}, and R^{10} is H, -PO_3M_x, -$(PO_3)_2M_y$ or -P(O)(alkyl)OM';

X^- is Cl^- or Br^-;

i) R^1 is H, R^2 is methyl, R^3 is -OH, R^4 is methyl, -CH_2OH or -CH_2NH_2, and R^7 is H;

ii) R^1 is -NH_2, -NHMe or -N(Me_2), R^2 is methyl, R^3 is H, R^4 is H or -CH_3, and R^7 is H;

iii) R^1 is -NH_2 or OH, R^2 is methyl, R^3 is H, R^4 is H, and R^7 is H;

iv) R^1 and R^3 are H, R^2 is methyl, R^4 is -NH_2, and R^7 is H;

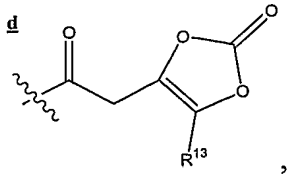
v) R^1 is -NH_2, R^2 is methyl, R^3 and R^4 are H, and R^7 is H, -CH(OH)CO_2H or -C(OH)(Me)CO_2H;

vi) R^1, R^3, R^4 and R^7 are H and R^2 is methyl; and

vii) R^1 is H, R^2 is -NH_2, R^3 is -OH, R_4 is -$CH_2CH_2NH_2$, and R^7 is H.

2. The compound of 1, wherein R^{10} is -C(O)R, -C(O)N(R_2), -C(O)OR, -$(CH_2)_{1-6}$-C(O)R, alkyl, carbocyclyl, aryl, heterocyclyl, heteroaryl, carbocyclylalkyl, aralkyl, heterocyclylalkyl, heteroaralkyl, or a tumor-targeting moiety; and R^{12} is -C(O)R, -C(O)N(R_2), -C(O)OR, -SO_2R, -SO_2N(R_2), carbocyclyl, aryl, heterocyclyl, heteroaryl, carbocyclylalkyl, aralkyl, heterocyclylalkyl, heteroaralkyl or a tumor-targeting moiety.

3. The compound of 1, wherein R^{10} or R^{12} is a polysaccharide, $-[C(O)CH(R)N(R)]_{2-3}-R$, an antibody, or



, wherein R^{13} is H, alkyl, or aryl.

4. The compound of 1, wherein said compound has one or more features selected from the group consisting of:

i) R^1 is $-(CH_2)_{1-6}N(R°)_2$, $-(CH_2)_{1-6}OR°$, -NRC(O)R, $-C(O)N(R)_2$, -CN, $-N(R)SO_2R$, -COOR, -SR, -C(O)R, halo, -OC(O)R, -NRC(O)OR, $-OC(O)N(R)_2$, $-N(R)C(O)N(R)$, -NRC(S)NR, $-NRSO_2NR$, $-C(O)NRN(R)_2$, heteroaryl, or heterocyclyl;

ii) R^2 is H, fluoroalkyl, -C(O)R, -COOR, $-C(O)N(R)_2$, -CN, -NRC(O)R, -OR, -SR, $-N(R)_2$, $-(CH_2)_{1-6}OR°$, $-(CH_2)_{1-6}N(R°)_2$, or halo;

iii) R^3 is alkyl, fluoroalkyl, -C(O)R, -COOR, $-C(O)N(R)_2$, -CN, -NRC(O)R, -SR, $-N(R)_2$, $-(CH_2)_{1-6}OR°$, $-(CH_2)_{1-6}N(R°)_2$, or halo;

iv) R^4 is fluoroalkyl, -C(O)R, -COOR, $-C(O)N(R)_2$, -CN, -NRC(O)R, -OR, -SR, $-(CH_2)_{1-6}N(R°)_2$, or halo;

v) R^{10} is H, $-PO_3M_x$, $-(PO_3)_2M_y$ or -P(O)(alkyl)OM'; or R^{12} is H or C_{1-6} alkyl; and

vi) n is 1.

5. The compound of 4, wherein:

i) R^1 is $-(CH_2)_{1-6}N(R°)_2$, $-(CH_2)_{1-6}OR°$, -NRC(O)R, $-C(O)N(R)_2$, -CN, $-N(R)SO_2R$, -COOR, -SR, -C(O)R, halo, -OC(O)R, -NRC(O)OR, $-OC(O)N(R)_2$, $-N(R)C(O)N(R)$, -NRC(S)NR, $-NRSO_2NR$, $-C(O)NRN(R)_2$, heteroaryl, or heterocyclyl;

ii) R^2 is H, fluoroalkyl, -C(O)R, -COOR, $-C(O)N(R)_2$, -CN, -NRC(O)R, -OR, -SR, $-N(R)_2$, $-(CH_2)_{1-6}OR°$, $-(CH_2)_{1-6}N(R°)_2$, or halo;

iii) R^3 is alkyl, fluoroalkyl, -C(O)R, -COOR, $-C(O)N(R)_2$, -CN, -NRC(O)R, -SR, $-N(R)_2$, $-(CH_2)_{1-6}OR°$, $-(CH_2)_{1-6}N(R°)_2$, or halo;

iv) R^4 is fluoroalkyl, -C(O)R, -COOR, $-C(O)N(R)_2$, -CN, -NRC(O)R, -OR, -SR, $-(CH_2)_{1-6}N(R°)_2$, or halo;

v) R^{10} is H, $-PO_3M_x$, $-(PO_3)_2M_y$ or -P(O)(alkyl)OM'; or R^{12} is H or C_{1-6} alkyl; and

vi) n is 1.

6. The compound of 1, wherein said compound has one or more features selected from the group consisting of:

i) R^1 is H, $-N(R)_2$, alkyl, -NR°C(O)NR, -NR°C(O)OR, $-C(O)N(R)_2$, $-(CH_2)_{1-6}N(R°)_2$, -NR°C(O)R, -CN, -COOR, -OR, -SR, or halo;

ii) R^2 is H, alkyl, fluoroalkyl, -OR°, $-N(R°)_2$, or halo;

iii) R^3 and R^4 are independently H, alkyl, -OR, $-N(R)_2$, $-(CH_2)_{1-6}OR°$, or $-(CH_2)_{1-6}N(R°)_2$;

iv) R^7 is H, alkyl, fluoroalkyl, $-(CH_2)_{1-6}OR$, $-(CH_2)_{1-6}N(R)_2$, -NR°C(O)R, -C(O)R, -C(H)(OR)R, aralkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, or heteroaralkyl;

v) R^{10} is H, alkyl, -C(O)R, $-PO_3M_x$, -P(O)(alkyl)OM', $-(PO_3)_2M_y$, $-C(O)N(R)_2$, -C(O)OR, or a tumor-targeting moiety; or R^{12} is H, alkyl, -C(O)R, $-C(O)N(R)_2$, -C(O)OR, $-SO_2R$, 5-membered heterocyclyl, 5-membered heteroaralkyl, or a tumor-targeting moiety; and

vi) n is 1.

7. The compound of 6, wherein:

i) R^1 is H, $-N(R)_2$, alkyl, -NR°C(O)NR, -NR°C(O)OR, $-C(O)N(R)_2$, $-(CH_2)_{1-6}N(R°)_2$, -NR°C(O)R, -CN, -COOR, -OR, -SR, or halo;

ii) R^2 is H, alkyl, fluoroalkyl, -OR°, $-N(R°)_2$, or halo;

iii) R^3 and R^4 are independently H, alkyl, -OR, $-N(R)_2$, $-(CH_2)_{1-6}OR°$, or $-(CH_2)_{1-6}N(R°)_2$;

iv) R^7 is H, alkyl, fluoroalkyl, $-(CH_2)_{1-6}OR$, $-(CH_2)_{1-6}N(R)_2$, -NR°C(O)R, -C(O)R, -C(H)(OR)R, aralkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, or heteroaralkyl;

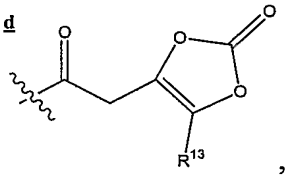
v) R^{10} is H, alkyl, -C(O)R, $-PO_3M_x$, -P(O)(alkyl)OM', $-(PO_3)_2M_y$, $-C(O)N(R)_2$, -C(O)OR, or a tumor-targeting moiety; or R^{12} is H, alkyl, -C(O)R, $-C(O)N(R)_2$, -C(O)OR, $-SO_2R$, 5-membered heterocyclyl, 5-membered heteroaralkyl, or a tumor-targeting moiety; and

vi) n is 1.

8. The compound of 6 or 7, wherein R is R°, carbocyclyl, aryl, heteroaryl, heterocyclyl, aralkyl, keterocyclylalkyl or heteroaralkyl.

9. The compound of 8, wherein R° is H or C_{1-6} alkyl optionally substituted with halo, hydroxy or amino.

10. The compound of 6 or 7, wherein R^{10} or R^{12} is a polysaccharide, -[C(O)CH(R)N(R)]$_{2-3}$-R, an antibody, or

d 

, wherein R^{13} is H, alkyl, or aryl.

11. The compound of 6 or 7, wherein said compound has one or more of the features selected from the group consisting of:

i) R^1 is H, amino, -CH_2NH_2, -NHC(O)NHEt, -NHC(O)OEt, -$NHCH_2OH$, -$NHCH_2CH_2OH$, -NH-CH_2CH_2Cl, -$N(CH_2OH)_2$, Cl, Br, -SCH_3, CN, -$C(O)NH_2$, -C(O)OH, methyl, or ethyl;

ii) R^2 is H, methyl, ethyl, amino, CF_3, Cl, or Br;

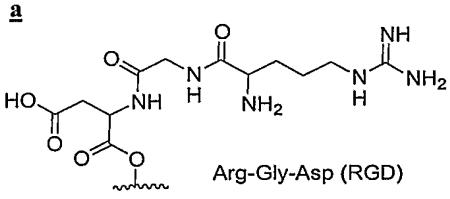
iii) R^3 is H, methyl, ethyl, amino, or hydroxy;

iv) R^4 is H, methyl, ethyl, -CH_2OH, or -CH_2NH_2;

v) each R^5, R^6 and R^8 is independently H, methyl, ethyl, -CH_2F, -CHF_2, or -CF_3;

vi) R^7 is H, methyl, ethyl, CF_3, -$CH(OH)CH_3$, -CH_2OH, or -CH_2CH_2OH; and

vii) R^{10} is H, methyl, ethyl, -C(O)Me, -C(O)Et, -$C(O)NMe_2$, -C(O)-p-OMe-phenyl, -C(O)O-phenyl, -PO_3H_2, -$P(O)(OMe)_2$, -P(O)(OMe)OH, -P(O)(Me)OH, -P(O)(OH)OP(O)(OH)(OH), or R^{14}; and R^{14} is selected from the group consisting of:

a 

Arg-Gly-Asp (RGD)

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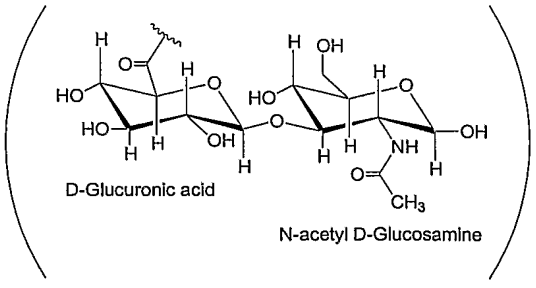
b 

D-Glucuronic acid

N-acetyl D-Glucosamine

poly

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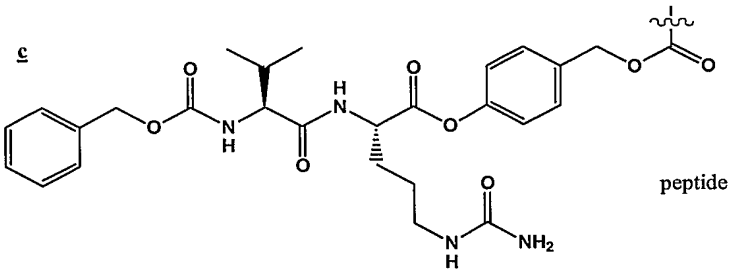
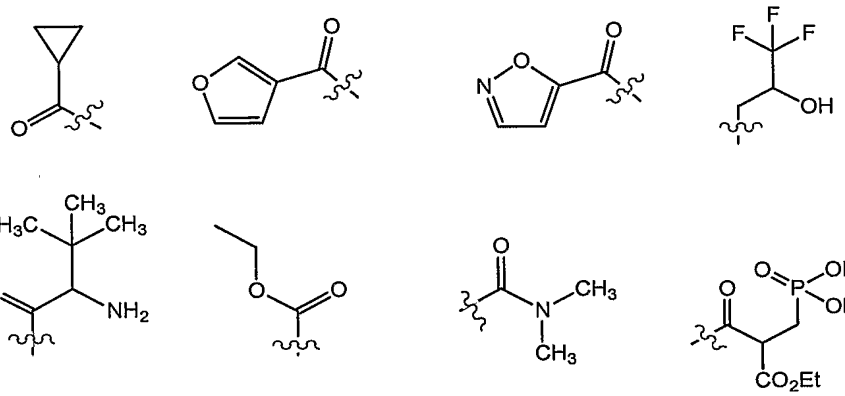
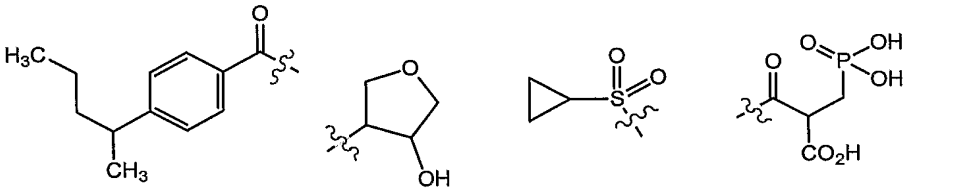
c

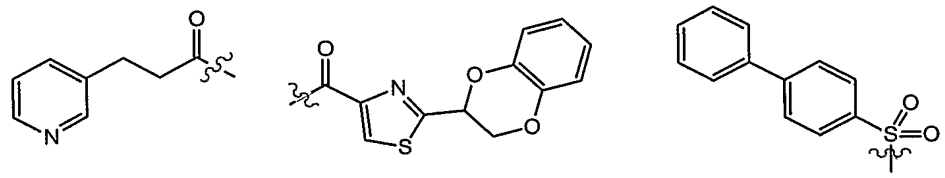


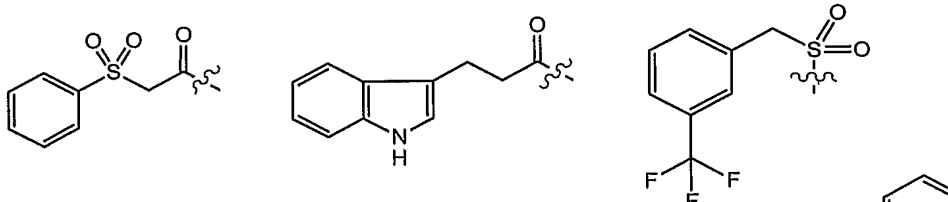
peptide Z-Val-Cit-PABOH

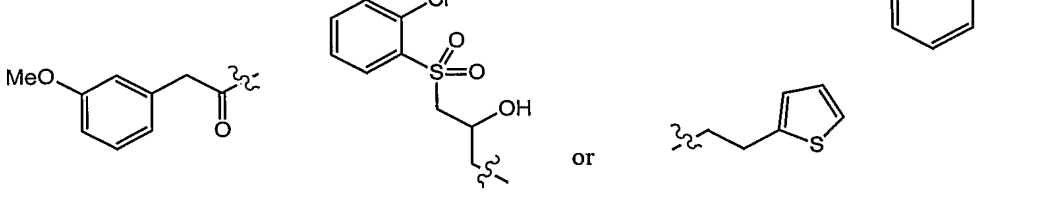
and an antibody; or R^{12} is H, methyl, ethyl, R^{14},











or

12. The compound of 6 or 7, wherein said compound has one or more of the features selected from the group consisting of:

i) R^1 is H, $-N(R°)_2$, $-SR°$, or halo;

ii) R^2 is H, alkyl, fluoroalkyl, $-N(R°)_2$, or halo;

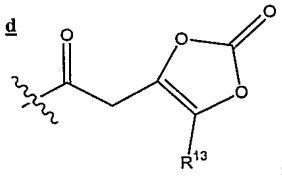
iii) R^3 and R^4 are independently H or alkyl;

iv) R^7 is H or alkyl;

v) R^8 is H or C_{1-6} unsubstituted alkyl; and

vi) R^9 is $-OR^{10}$ and R^{10} is H, C_{1-6} unsubstituted alkyl, $-C(O)R$, $-PO_3M_x$, $-P(O)(alkyl)OM'$, $-(PO_3)_2M_y$, $-C(O)OR$, or a tumor-targeting moiety.

13. The compound of 12, wherein R^{10} is a polysaccharide, $-[C(O)CH(R)N(R)]_{2-3}-R$, an antibody, or



, wherein R^{13} is H, alkyl, or aryl.

14. The compound of 12, wherein said compound has one or more of the features selected from the group consisting of:

i) R^1 is H, $-NH_2$, $-SCH_3$, or Cl;

ii) R^2 is H, methyl, $-CF_3$, $-NH_2$, or Cl;

iii) R^3, R^4, R^7 and R^8 are independently H or methyl; and

iv) R^9 is $-OR^{10}$ and R^{10} is H, H, $-PO_3H_2$, $-P(O)(OMe)_2$, $-P(O)(OMe)OH$, $-P(O)(Me)OH$, $-P(O)(OH)OP(O)(OH)(OH)$, or R^{14}; and R^{14} is as defined in 11.

15. The compound of 1, wherein said compound is **IIa-1**, **IIa-2**, **IIa-3**, **IIa-4**, **IIa-5**, **IIa-6**, **IIa-7**, **IIa-8**, **IIa-9**, **IIa-10**, **IIa-11**, or **IIc-1**.

16. A pharmaceutical composition comprising a compound of 1-15 and a pharmaceutically acceptable carrier.

17. The composition of 16, further comprising at least one chemotherapeutic agent, antiangiogenic agent or agent which modulates signaling associated with hypoxic conditions in a cell.

18. A method for inhibiting transketolase activity in a biological sample or a patient in need thereof comprising contacting said biological sample with or administering to said patient an effective amount of a compound of 1-15.

19. A method for reducing levels of ribulose/ribose-5-phosphate in a cell comprising administering to the cell an effective amount of a compound of 1-15.

20. A method for inhibiting nucleic acid synthesis in a cell comprising administering to the cell an effective amount of a compound of 1-15.

21. A method for inhibiting cell proliferation comprising administering to the cell an effective amount of a compound of 1-15.

22. A method for increasing apoptosis in a tumor cell comprising administering to the cell an effective amount of a compound of 1-15.

23. A method for reducing tumor growth in a patient comprising administering an effective amount of a compound of 1-15 or a composition of 16 to the patient in need thereof.

24. The method of 23, further comprising administering at least one chemotherapeutic agent, antiangiogenic agent or agent which modulates signaling associated with hypoxic conditions in a cell.

25. The method of 23 or 24, further comprising limiting thiamine concentrations in the patient during the administration step.

26. The method of 25, wherein the patient is on a reduced thiamine diet during the administration step.

27. The method of 26, wherein cellular thiamine concentrations are maintained at a level sufficient to avoid toxicity associated with thiamine deficiency.